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## Minutes

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Concerning:	<b>Development Committee Meeting, Basel 12.04.2005</b>		

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**Main Points:**

**Thiamethoxam/Actara project portfolio:** With \$17.5 m in 2005, development spend on this AI is still high; the chosen strategy will ensure that products are well positioned ahead of the advent of generic imidacloprid.

**Cruiser ST development strategy:** Segment specific offers are developed to cope with future competition and price differences between market segments.

**Azoxystrobin formulation projects:** New formulations aimed at growth opportunities in developing markets and migration towards mixtures in developed markets will defend position as market leading fungicide.

**Mesotrione carry-over effects in soya:** The issue is now well understood and problems that may occur under rare circumstances in specific situations can be identified early.

**Ametryn registration in USA:** Assuming data demands from EPA are within expectation, it is proposed to defend the full registration at a cost of about \$4-6 m und thus future sales of ca. \$35 m.

**Development and distribution of pyribenzoxim-based products:** DeCo supports the proposal to work with this 3rd party product from LGLS/Korea and to develop products for broad-spectrum weed control in direct seeded rice in Southeast Asia and Latam.

**1. Minutes of the last meeting**

Action: 4.2: SYN 517'627 should no longer be viewed as an alternative to SYN 520'543 as there are now more attractive candidates available.

L. Smith informs that the possibility of using tebuconazole as a partner in seed treatment products is currently under consideration as an alternative to developing a new proprietary AI. The SYN 508'210 team is asked to maintain awareness of this initiative; the focus of the ongoing program should be on defining the biological profile. Review will be required before significant investments are sanctioned for the tox programme.

**2. Thiamethoxam/Actara: Project Portfolio Review**

The portfolio was presented by E. Molitor, T. Kelly, F.Quiroga, R. Senn, J-F. Hecquet, supported by M. Stepan and R. Claveano

The objective of the session was to up-date DeCo on the development strategy for thiamethoxam and to display the status of the most important projects.

**Development objectives:**

- Exploit the USP's of TMX alone and in mixtures through crop offers and differentiate from other neonicotinoids
- Take the lead position in soil application in high value crops with mixtures.
- Grow market share in broad spectrum field crops segment through mixtures: Engeo \$52 m by 2009 in OP's replacement markets
- Build a world-class umbrella brand.

Sales of Actara continue to grow; some key countries are still in the pre-launch or launch phase:

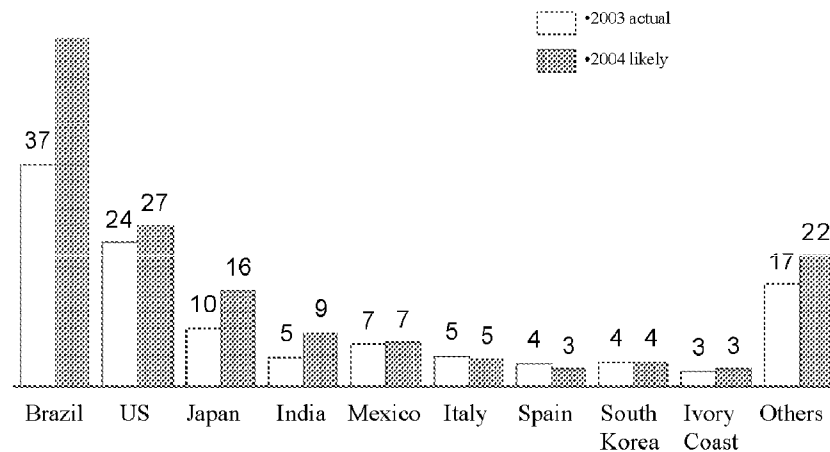
2004: AME, Egypt, Portugal and Japan launches

2005: Engeo in LATAM

2006: Actara France, 2007: UK and Germany

2007: US, Canada Q\* resolution

Sales of Actara (\$ m)



Generic imidacloprid is expected to appear as a competitor to TMX in several markets and it is important to use the next 2-3 years to differentiate TMX effectively from imidacloprid. From 2013 onwards we are likely also to lose the exclusivity of TMX.

A key objective of the post-patent strategy is to achieve meaningful market segmentation by identifying segments where TMX has a potential competitive advantage and where it provides a differentiated offer. This should enable us to optimise value and market share.

Current and future offer by segment (Market size 2003, \$ m)

•Segment	•Crops	•Current offer	•2009/10 Future offer	•Rationale/advantage over existing offer
Soil systemic insect control •150	– Vegetables, tobacco	– Actara 25WG – Actara 1.5 Gr – Actara 0.5 GR	– Actara + Tefluthin – Slow release formulation	– Broader spectrum -replace OPs/OCs – Better uptaken/Longer residual – Improve regulatory - lower leaching risk – Formulation IP
	– Potatoes			
Foliar sucking insect control in high-value crops •720	– Vegetables, tobacco	– Actara 25WG	– Actara + Abamectin	– Superior thrips control
	– Potatoes	– Actara + Lufenuron	– Actara + Lufenuron	– Formulation IP
Foliar sucking insect control in other crops •150 + 30*	– Fruits/nuts	– Actara 10 SG	– Actara high strength	– Fighting Brand
Foliar broad spectrum insect control •450	– Cotton	– Centric 40WG	– Actara high strength	– Fighting Brand
	– Rice	– Actara 25WG – Actara 240 sc	– Actara + Cartap	– Complete rice offer
Foliar broad spectrum insect control •450	– Field crops	– Actara 25WG	– Actara + Lambda	– Complete the offer-Segments
	– Fruits and veggies	– Actara + Lambda – Actara + Lambda K	– Actara + Indoxacarb	– Formulation IP – OP's replacement opportunity
Insect&disease control in high value crops •140	– Rice			
Insect&disease control in other crops •40+100	– Vegetables, tobacco	– Actara + Mefenoxam	– Actara + Azoxystrobin	– First Mover advantage
	– Potatoes		– Engeo+AmistarXtra?	– LCM- Extend Patent Protection
Insect&disease control in other crops •40+100	– Tropical plantations	– Actara + Pyraquilon	– Slow release formulation	– Cost positioning
	– Rice	– Actara + Cyproconazole	– Actara + Cyproconazole	– Broaden spectrum – Longer lasting – Formulation IP

### Formulation Development Projects

- a) Thiamethoxam (0.5%)+ tefluthrin 0.5%) soil applied granule formulation against soil- and early season sucking and feeding foliar pests
- Status
- o Formulation developed locally for Japan (A-14126B)
  - o Formulation adaptation to „global“ cheaper Korean carrier successful (A-14126C)
  - o Final registration phase in Japan (sales in 2006)
  - o Field and residue trials in EU ongoing
- Innovation potential
- Modern compound for OP/carbamate replacement in cabbage and early season vegetables
- Technical Issues
- o Risk to exceed EU groundwater limit of 0.1 microgr/ L
  - o Inherent Skin Facial Sensitisation Risk through dust
  - o Specific application machinery needed for proper placement
- b) Actara controlled release product for soil use offering increased persistence of effect combined with reduced mobility/leaching
- Status
- o 5% hot extrusion granule (most advanced technology for controlled release)
  - o 75 CS (however sprayable formulation is preferred)
  - o Hand-over from Performance Enhancement Research to Development in December 04
  - o Broad field testing on stations
  - o Small scale lysimeter study at planning stage (EU)
- Innovation potential
- o Reduce leaching of AI and product loss
  - o Increase persistence after soil application
- Technical Issues
- Technical feasibility, patent limitations
- c) Actara High-strength formulation (~ 40-70 SG) for the foliar market as a cost effective long-term alternative to Actara 25 WG
- Status
- Idea Evaluation within formulation group; no field work yet
- Innovation potential
- Cost reduction
- d) Engeo SC (141 g TMX + 106 g L-cyhalothrin / l) cost-effective foliar applied broad-spectrum product for the control of chewing and sucking pest (replacement of monocrotophos)
- Status
- o Stage C promotion in 2Q/03 in Brazil
  - o First sales in Argentina and Paraguay; Brazil 1Q'05
  - o Started field trials in NAFTA '05
  - o Field trials and registration activities in APAC and EAME
- Innovation potential
- o OP replacement offer
  - o Competitive pricing
  - o Delivering new AIs, novel formulation technology (Zeon), broad labels, broad MRLs/import tolerances
- Technical Issues
- o Fast tracking development to maintain innovation leadership in the segment
  - o Technical positioning to minimize cannibalisation of Actara and Karate

- e) Verdadero WG60 (300 g TMX plus 300 g Cyproconazole / kg) soil applied broad-spectrum product for the control of coffee rust and leaf miners
- Status                      o Sold in coffee in Brazil; field testing of opportunities in soybean (soybean rust plus stink bugs)
- Innovation potential    o Long lasting combination product (insecticide plus fungicide) for soil application in coffee  
                                 o Highly concentrated formulation  
                                 o Only neonicotinoid in coffee; no similar product (fungicide plus insecticide)
- Issues                      Low interest outside Brazil
- f) Digital Coratop Actara GR14 (2% TMX plus 12% pyroquilon) for full season insect and rice blast control in the rice seedling box in Japan.
- Status                      First sales in Japan in 2004
- Innovation potential    o Slow Release Formulation technology (pan-coating)  
                                 o Pyroquilon only fungicide in Japan without cross resistance  
                                 o To differentiate from new comers such as BASF strobi plus clothianidin
- Technical Issues        o Phytotoxicity risk of pyroquilon  
                                 o Formulation costs are currently high; the switch to a hot melt extrusion granule is under consideration

#### Regulatory

Actara and related brands are now registered in 92 countries on 94 crops. The plan is to obtain registrations in a further 6 countries by the end of 2009.

In **APAC** and **Latam** products are registered in all key markets and the focus has shifted to extending labels and registering additional formulations. No issues or restrictions are expected with the registration of any of the new mixtures.

In **NAFTA** Actara is registered in the USA and Mexico but Q\*-based risk assessment limits the current label.

The objectives are to

- Register Actara in Canada by the end of 2006 (last country in the Americas)
- Maximise the Label Extensions (via removal of Q\*; expected by 2007) and expand the soil uses in order to differentiate from imidacloprid, acetamiprid and generics
- Explore and register according to the minor use program in the USA in order to gain additional period of data protection

The issues remains the Q\*, the FQPA extra safety factor and leaching (as long as Q\* exists)

In **EAME** developments were initially held back by the patent conflict with Bayer, but Actara is now registered in Austria, Italy, Portugal and Spain.

The key objectives are

- TMX EU Annex I inclusion in 2006 with the most favourable classification and labelling in order to achieve the best position versus competition and in the eyes of the public
- Registration of Actara in France in 2006 - the business driver in W-EU
- Registration of TMX+tefluthrin granule in F, UK, NL, D and B within 5-7 years
- Maximization of Label Extensions

The leaching potential to groundwater of TMX remains an issue in W-EU, as is the potential environmental concentration in surface water in view of the toxicity of the AI to non-target organisms. Further potential hurdles (particularly in France) are the toxicity to bees of dust from granules.

Currently incomplete product offers – expected formulation and label extensions:

Country	Crop	Registration	Time
Canada	Potatoes	New	2006
France	Peach, apple, fruiting/ leafy veg.	New	2006*
Germany	Potatoes (leaching issue)	New	Subm. 05
Greece	Pome fruit, fruiting/ leafy veg., potatoes, tobacco, cotton...	New	2005
NL	Ornamentals	New	
UK	Potatoes	New	Subm. 05*
USA	Cole crops, leafy vegetables	LEX	2007
Mexico	Cole crops, leafy vegetables	LEX	2007
France	Cucurbits (soil only), grapes	LEX	2006*
Greece	Beans	LEX	
Italy	Beans, cabbages?, grapes, Vegetable (Indoor)?, cab- bages?	LEX	
Portugal	Fruiting/ leafy veg. – soil applications, grapes	LEX	2005-2006
Spain	Lettuce?, Citrus (bearing), beans, cabbages, grapes?	LEX	

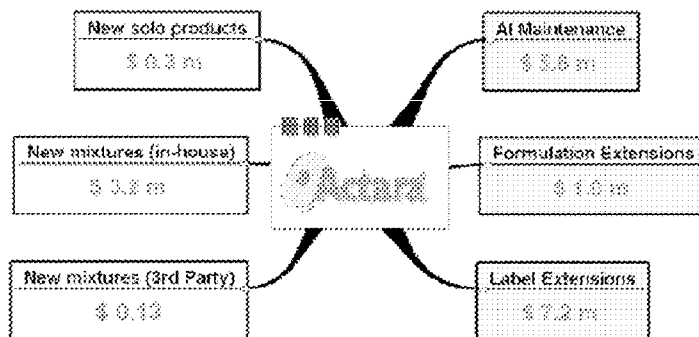
Milestones for the new products

		2005				2006				2007				2008				2009				2010			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Broad Spectrum IC	Engeo																								
	Latam		★																						
	APAC									★															
	Nafta													★											
Soil Systemic IC	TMX+ tefluthrin																	★							
	ControlledRelease																							★	
Foliar & Sucking IC	High Strength																								
	TMX/cartap																								
Insect & Disease Control	Verdadro	★																							
	TMX/probenazole									★															
	DCA hot Extr.																	★							
		<div>PER</div> <div>Stage C</div> <div>Idea Evaluation</div> <div>Registration</div> <div>Stage B</div> <div>First Sales</div>																							

#### Development investment

	First Sales	Target Sales (\$m)	NPV @ 16% (\$m)	Dev Cost in 05 (\$m)	5y Dev.Cost (\$m)
Engeo	2005	90	87+	1.7	3-5
Verdadero light	2005	19	30	0.06	0
TMX plus tefluthrin	2009	12	29	1.0	4-5
Digital Coratop Actara	2008	14	20	0.4	3-4
Controlled release	2009/10	30	n.a.	0.4	5-10
<b>Total</b>		<b>165</b>	<b>166</b>	<b>3.6</b>	<b>15-24</b>

The total investment for 2005 in support of the Actara Development Project Portfolio which is forecast to ultimately deliver sales of \$321 m is \$17.5 m



#### Discussion and conclusions

Although sales have started in 1997, considerable investments (estimate: \$40 m to peak sales) are still needed to exploit the full potential of the molecule. Development was hampered by the patent conflict with Bayer (Europe) and the Q\* risk assessment in NAFTA and in some cases sales build-up was dependent on the authorities willingness to regulate OPs. Some of the combination products only emerged as a result of the merger.

The advent of generic imidacloprid is likely to mean more intense competition and price pressure; efforts aimed at identifying market segments where thiamethoxam-based products can be competitive are welcome and deemed necessary. Attention also needs to be paid to the risk of resistance building up in segments where generic imidacloprid may be widely used in due course. Whilst we have a resistance avoidance strategy, albeit one that is not harmonised with the one Bayer follows, it must be assumed that the suppliers of generic material will not pay attention to this aspect. Regulatory authorities and customer groups appear to be natural allies in attempts to safeguard the effectiveness of the neonicotinoides. The plan is to indicate the mode of action of the label and to lobby that newcomers are forced to do the same to enable farmers to make informed decisions.

Soil application through drip-feeding is confined to southern Europe and to greenhouses. This means that irrigation is controlled and the risk of leaching correspondingly low. Whilst we already have good data for modelling behaviour following conventional soil application, further efforts will be required before we have reached the same position with drip application.

Formulation development for the rice segment is slowly being wound down as collaboration with Japan is now closer and recognition has set in that budgets are limited. Some modifications are required to enable us to achieve acceptable profit margins and there is still a project running in



Performance Enhancement Research aimed at achieving controlled slow release. If successful this is expected to help in Europe (soil mobility) and by extending the efficacy in rice and sugar cane.

Predicted long-term development spend appears reasonable (if forecast sales materialise), but current levels of > 9% of sales are still high for an AI that is well into Stage 4 (note: part of the AI maintenance cost will also benefit Cruiser).

The advent of the bisamids has not yet been factored into future sales as the focus so far has been on capturing the likely impact of generic imidacloprid.

The question was also raised of whether there could be any advantages to us in working with generic imidacloprid ourselves. The team showed little interest in the concept on the grounds that with the new and very innovative formulation concepts we have a 2-3 year first mover advantage opposite competitors and that we should not jeopardise this by diluting our efforts at present.

- 2.1. Decision: The proposed strategy is supported on the assumption that all new formulations meet existing hurdle criteria. J. Barnes
- 2.2. Action: Further attention should be paid to the likely effect of generic imidacloprid on the development of resistance to neonicotinoids with a view to adjust our strategy as appropriate. K. Gehmann
- 2.3. Action: Efforts should be undertaken to fully understand the implications of drip application for surface and ground water. H. Swaine
- 2.4. Recommendation: Marketing is encouraged to consider the influence of the bisamids and the new Bayer sucking pest compound on sales forecasts. M. Stepan
- 2.5. Action: Given the novelty of some of the new formulation concepts, careful consideration should be given to any opportunities to protect the intellectual property as it relates to our own, but also other manufacturers compounds. K. Gehmann

### **3. Seed Treatment: Cruiser ST: Development strategy and review of key new formulation projects**

Presented by: T. Kelly, F.Quiroga, J-F. Hecquet, R. Claveano. Guests: M. Stepan and E. Molitor

#### **The market:**

The neonicotinoid market is expected to grow at a compound annual growth rate of over 9.5%.

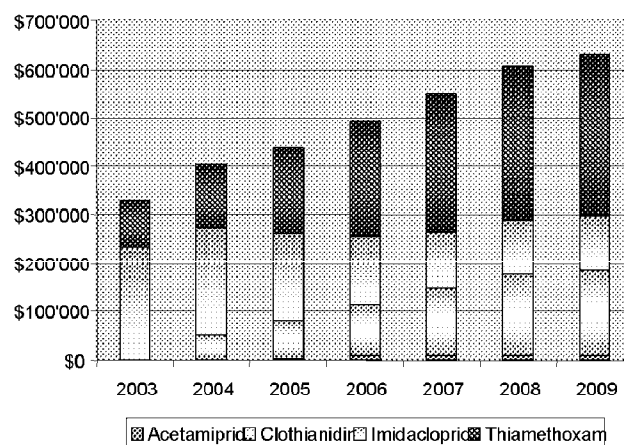
A majority of this growth will come from CRUISER.

The objectives are to exceed \$275m in sales by 2008:

- \$80m in soybeans
- \$65m in corn
- \$20m in sugar beets

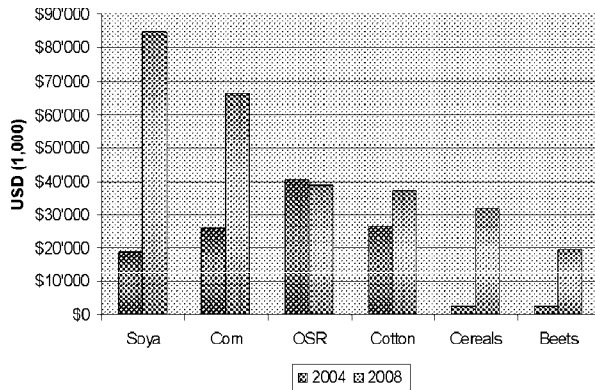
and for Syngenta to become the primary supplier for Key Accounts.

The majority of sales will come from





the following crops (~ 90%):



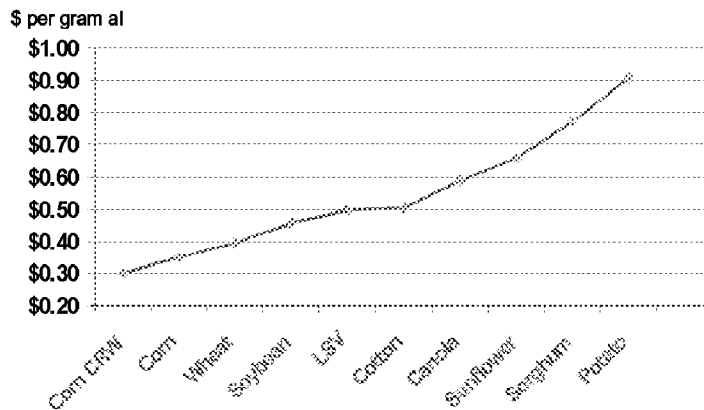
... and the following key countries (~80%) by 2008:

- USA ca. 30%
- Brazil 22%
- France 15%
- Canada 10%
- Germany 4%

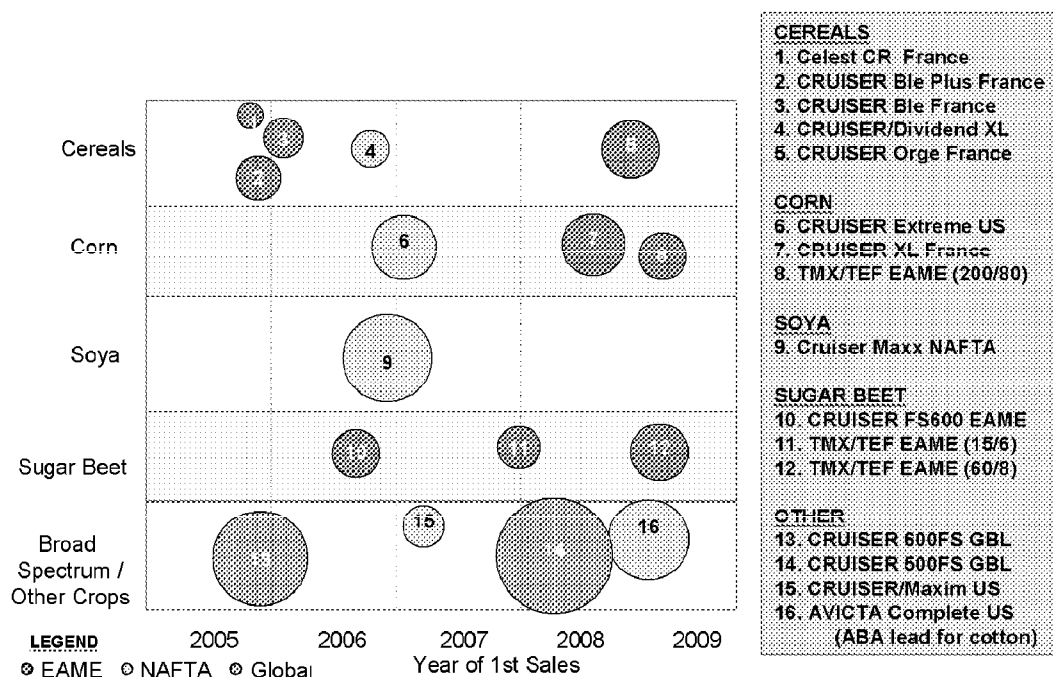
The planned sales will be achieved through the development of segment-specific offers for CRUISER. This will enable us to capture a larger portion of the market and will shield us from generic imidacloprid.

Part of these offers will be a lower priced TMX product for corn and sugar beet in Europe and a formulation with fungicides for soybeans, corn or cotton in Brazil. We will also explore different brand options/formulations to achieve greater reach in Africa, Middle East and APAC.

A further reason for differentiation is the significant differences between the bearable price in different segments:



Dev Portfolio 2005 to 2010 (bubble size = final target sales)  
delivering the segmentation strategy:



#### Key projects:

##### a) Thiamethoxam + Tefluthrin mixtures for EAME

**Objective:** To develop a low and high tier offer allowing Syngenta to maximize revenue and extend the reach of the brands in maize and sugar beet.

- Market: European maize and sugar beet
- Projected sales: \$30 m - \$20 m in sugar beet and \$10 m for use in corn
- Market share expectations: maize 15% and sugar beet 30%.
- Maize competition: Poncho 600FS, Gaucho 600FS
- Sugar Beet competition: Imprimo, Montur. Future competitors include Poncho Alpha and Beta (clothianidin + Beta cyfluthrin).

	Sugar beet	Maize
Low Value Segment (soil pests)	Cruiser Force 15+6 (\$5 m)	Cruiser Force 250 (\$7 m)
Mid-Tier Segment (soil and foliar pests)		Cruiser (\$10 m)
Mid-Tier Segment (soil and foliar pests)	Cruiser Force 60+8 (\$15 m)	Cruiser Force 1000 (\$3 m)

#### Thiamethoxam + Tefluthrin EAME Maize: Project status:

- The focus was on candidates with addition of FORCE 20CS to the „Diamond“ variants of CRUISER with additional colorants/polymer; several formulation related issues to be overcome prior to freeze
- Variants have been lab and field-tested for efficacy and safety in 2004 and 2005 at a range of rates; no issues from a biological perspective so far - need confirmation in 2005. Some bird repellence observed, a nice to have. To be investigated further in 2005, early results look promising.

- Two use rates to be registered; high tier segment/*Diabrotica* 1/0.4 mg AI per seed (100-120 g AI/ha TMX), low value segment (soil pests) 0.25/0.1 mg per seed
- Submission timelines will be different because field studies for earthworm and non-target arthropods will be needed to support the high rate.

Issues:

Risk	Likely solution
Smell of the solvent in FORCE 20CS may be too strong for the maize market.	Avoid – If odour proves unacceptable -> address via FORCE 20CS re-formulation
Seed Storage: AI volatility/loss of AI on treated seeds; known issue with tefluthrin	Avoid – understand and make practical recommendations. Use of a polymer at application?
Addition of an absorbing powder dust at application is not acceptable from a regulatory/safety perspective. Powder definitely needed at high rate. Increases likelihood of dust off issues.	Avoid – Perform operator exposure assessment prior to freeze. If a solution cannot be found the use of a higher tefluthrin concentrate could be considered.
It is decided to re-formulate the FORCE 20CS product.	Accept – Obtain better understanding of 20CS proposals prior to freeze. If reformulation goes ahead some work may need to be repeated.
Regulatory: The high rate of 1/0.4 mg AI/seed is not registrable in all countries.	Accept – Monitor developments; test case with NL.
Biology: 2005 trials do not confirm the expected/required efficacy from the product on <i>Diabrotica</i> , key pests	Avoid – Assess prior to freeze. If a significant issue then candidate would not be frozen.

#### Thiamethoxam + Tefluthrin EAME sugar beet

The focus has been on adding FORCE 20CS to the CRUISER FS600 SB formulation. Target use rates are:

Low Tier: 15/6 g ai/100'000 seeds

High Tier: 60/8 g ai/100'000 seeds (60-80 g AI/ha TMX)

Two candidates for each project have been tested for germination by seed companies. They were at least equivalent to co-application of CRUISER/FORCE and the competition.

There is a partnership with 3 seed companies for ongoing lab testing.

Lead candidates will be field tested for efficacy/safety in 2005 to confirm the good 2004 results.

The issues and risks are similar to the ones that exist for maize.

#### b) NAFTA pre-mixes

##### CRUISER Maxx

Objective: To develop a single offer for US soybeans to maximize revenue and share while protecting the higher value corn markets.

- Projected revenue: > \$32 m; market share expectations: >80%
- Competition: Gaucho 600FS

Formulation frozen in 1Q '05; selection based on *Rhizobia* friendliness, acute skin and eye, and physical and chemical stability results.

Formulation concentration 255 g AI TMX +13 g AI fludioxonil + 19g AI mefenoxam per litre.

Originally driven by USA need, but Canada have now joined the project and the regulatory package will now be for NAFTA.

There are no known issues for formulation, biology or regulatory at present.

### CRUISER Extreme

Objective: To offer a unique product for US corn to maximize revenue and market share.

- Projected revenue: > \$18 m
- Market share expectations: > 25%
- Competition: Poncho 600FS

Formulation concentration 307 g AI TMX + 15 g AI fludioxonil + 12.5 g AI mefenoxam + 6 g AI azoxystrobin per litre. Submission to the EPA in June 2004; registration expected by end of 2Q '05.

There are no known outstanding issues for formulation, biology or regulatory at present.

### CRUISER 500FS and 600FS (Project Diamond; all regions/multiple crops)

Move to two Global Formulations by 2010 and eliminate the current 350 FS, 70 WS (coloured), and 5S:

- CRUISER 500 FS coloured formulation for Europe, LATAM, APAC, Canada and other markets in need of a coloured formulation. Currently being developed in Basel. Expected sales: \$80m; formulation was frozen in April 2004. Regulatory package will be complete 2Q'05.
- CRUISER 600 FS is a non-coloured formulation for NAFTA, Australia, China and other markets not needing a coloured formulation. Currently being developed in the US. Expected sales: \$35m; Submitted to the EPA in Nov 2004 - US registration expected by end Q3'05, 1st sales 2006.

The market share for the two products is forecast to be >38%; the main competition will come from Poncho 600FS and Gaucho 600FS.

### Benefits of the new formulations

- The low dust-off benefit of the CRUISER 500FS is a clear benefit to operators and farmers, but more importantly to various governmental regulatory agencies.
- Opportunity to differentiate from Bayer products
- Supply chain improvements
- More robust to different AI properties and water qualities
- Potential of IP protection being investigated
- Use of polymer to reduce dust off
- Move to a higher strength formulation

### CRUISER – new ideas under evaluation

- New market segmentation product(s) for Brazil for corn, cotton and possibly soybeans.
  - o Projected revenue (not incremental) >\$35m
  - o Market share expectation >40%
  - o Workshop in June 2005 to discuss way forward
- Potential low cost solutions for APAC/E EU/AME
  - o Mixtures with L-cyhalothrin/or solo
- Testing agreement for fipronil in 2005
  - o US; Corn Root Worm
  - o EU/RSA; corn
  - o Australia; cotton and canola
- Product Enhancement Research; slow release TMX formulation
  - o First priority to increase activity (lower rate) vs. *Diabrotica*
  - o New technologies to be field tested in 2005 in Research

Overall Registration status and plan

Country	Cotton	Maize	Sorghum	Sunflower	Wheat	Barley	Rape	Sugarbeet	Potato	Vegetable	Soya
Australia	A	A	A								
Argentina	A	A		A							
Austria		A						A			
Brazil	A	A			A	A			A		A
Canada		Q2 05	A		Q2 05	Q2 05	A				
France		2008		???	Q3 05	Q3 05	2008	Q4 05		D	
Germany		A					A	A			
Great Britain (UK)					Q2 06	Q2 06	Q3 05	Q3 05		D	
Spain	Anl	Anl						Anl	A	D	
United States	A	A	A	A	A	A	A		A	D	A

approved



pending



in development



Anl

Post Annex I

**Issues:****Bees/ precautionary principle in France:** additional bee studies lasting several years initiated**Pesticide drift and leaching in France:** modelling submitted, Cruiser 500FS Diamond project (ongoing)**Ground water/surface water contamination in EU:** monitoring may be required**Discussion and conclusions**

The proposed strategy of developing a significant number of new, mainly combi products, represents a departure from the past; currently almost 75% of sales are achieved with single formulations. Given the differences in price levels between crops and the advent of new competition, the new approach appears a promising way forward. It was reassuring to hear that many of the formulations were based on a standard technology platform and that the impact on formulation development resources and supply logistics would be manageable. The opportunity for differentiation appears best in soybean where we are able to exploit the vigour effect and yield increases achieved with thiamethoxam, but not with imidacloprid and clothianidine. The sugar beet and corn seed markets are influenced by dominant seed companies and our ability to shape the market is limited. In cereals, decisions are made closer to the grower and opportunities for tailored offers exist.

The bird repellence effects observed are interesting and may be viewed favourably by growers. Before making any claims, however, potential reactions from ornithologists need to be considered carefully. They could interpret this is a sign of sub lethal effects and ask for more studies. Regulatory progress in some countries (e.g. UK and France) is hampered by resource constraints within the agencies, but the expectation is that approval in France will be achieved in summer or by autumn '05 at the latest.

The bee issue is not an issue outside France, and the Germans in particular do not appear unduly worried. Ongoing studies there may also prove useful in France.

The team is aware of the potential risk of SFS (subjective facial sensation) effects occurring due

to the presence of tefluthrin; no adverse observations have been made to date, but monitoring continues and results will be factored into the operator safety risk assessment. The team was encouraged to assess resource requirements carefully and to phase projects in a way to achieve early market entry with those formulations selected for funding.

- 3.1. Action: Consider opportunities for patenting the observed bird repellency effect, but also assess possible reactions from regulators and ornithologists.

J. Street/25.10.05

- 3.2. Action: Consider whether the use of generic imidacloprid as a mixing partner (in addition to TMX) could improve the overall performance, cost-effectiveness and the profit margin of products. K. Gehmann/15.6.05

- 3.3. Action: OP-based products are still widely used in some segments and the scope for obtaining regulatory support for substituting modern products more quickly should be explored. J. Street/13.12.05

#### 4. Azoxystrobin: Formulation Project Review

The topic was presented by P. Varney, H-J. Kempf and A. Leadbeater

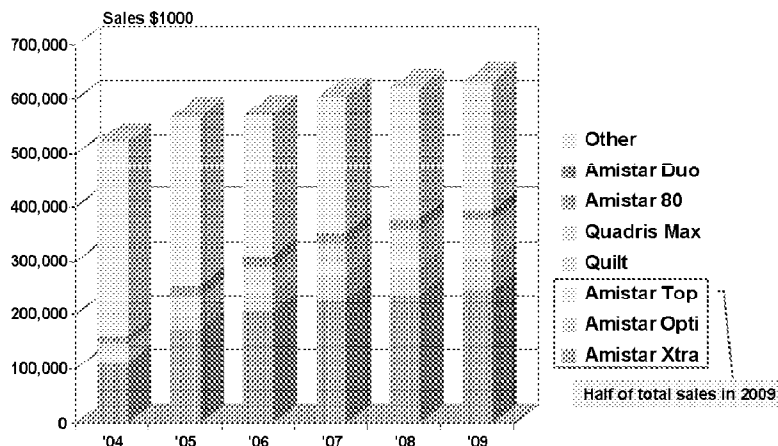
A number of formulations are in development:

	Product	Number of formula-tions	Number of regis-trations granted	
1.	Priori / Amistar Xtra ( Az + Cyproconazole)	1	8	<ul style="list-style-type: none"><li>- Mature projects which started in 2001</li><li>- 1st registration in 2003 (Amistar Xtra in UK) for Product Life Cycle Man-agement</li><li>- Remaining activities mainly in areas of Registration (submissions until 2008) and Field Development with resources of \$5.8 m total in 2005</li></ul>
2.	Quadris / Amistar Opti (Az + Chlorothalonil)	3	4	
3.	Amistar Top (Az + Difenconazole)	1	2	
4.	Amistar Duo / Quilt (Az + Propiconazole)	2	3	

#### Development objectives:

- To maintain position as market leading fungicide globally (>\$500m 2004)
- To exploit growth opportunities in developing markets; soya (Latam/US), cereals (E. Europe, NAFTA, Latam, Australia), vegetables (APAC)
- Maintain high level of brand equity in developed markets and improve in key markets where currently weak

#### Expected Sales:





- Introduce mixture products. Migrate business towards mixes in key markets to maximise azoxystrobin use and defend against competitor activity.

Migration of the business towards mixes in key markets is expected to help maximise azoxystrobin use, to manage resistance and to defend against competitor activity.

Some products are needed for specific segments:

- Quilt (+propiconazole) is useful where cyproconazole is not available (e.g. Scandinavia) or where a low-cost product is needed (US)
- Priori Extra (+cyproconazole) is an excellent product against rust in soya
- Amistar Opti (+chlorothalonil) is the best choice in *Septoria*-resistant cereals

There are also some crop- and Region-specific objectives:

Soybean:

- Biological profiling for US: spray programs with Tilt, Quilt, Alto and Quadris. Trials in AR, BR and USA
- Crop oils: Nimbus rate adjustments, substitution
- Application technology: Spray volume reduction, nozzles, ULV
- Label extension: *Rhizoctonia*, *Anthraco*

Wheat:

- Development: Eastern Europe
- Take-All: France, Germany

Others:

- Cotton, peanut, OSR, maize, coffee: New uses, segmentation, competitor threat, resistance management

APAC:

Rice, fruit, vegetables

- Biological profiling and registration trials

EAME:

Cereals

- *Septoria tritici*

Veggies

- Substitution of Ortiva in FR, BE, UK, SP, IT, PT
- Leek, tomato, lettuce, carrot, Brussels sprout, cabbage
- Peas, beans, onion cauliflower vs. boscalid

Arable crops

- OSR, sugar beet. Performance, yield / yield quality, physiological effect vs. boscalid

Latam

- Soybean: spray program in low rust pressure situations
- Fruit and vegetables: label extension

A key success factor still is to develop the US soya business following the identification of Asian Rust; there is a need to establish quickly in the new market. The key product in the short term (2005) is Quilt and from 2006 and beyond it will be Quadris Xtra (+cyproconazole). There is still a chance that we will be able to sell Quadris already in '05 under a Section 18 approval.



## Discussion and conclusions

The azoxystrobin programme has generally been very successful: High sales exceeding forecast have been achieved with Amistar Xtra and Quilt. Amistar Opti and Amistar Duo have been brought to the market in a very short time and with Amistar Opti we have been successful in defending the market in the UK.

The cost for developing these new formulations will be about \$6 m in 2005 (out of a total spend of about \$11 m for azoxystrobin). About 75% of the spend on new formulations is in field development.

In view of expected sales of more than \$ 600 m the investment appears justified.

Work on a comprehensive post-patent strategy is ongoing and results are expected by the end of May '05. The Gap Analysis done by McKinsey has identified *Fusarium* in cereals as an opportunity; although not very big, it is interesting because of the micotoxin issue.

There is some concern about the occurrence of resistance of net blotch in barley, but the impact is expected to be small since effective mixture products are available. There are also some indications of resistance developing in *Sigatoka* in banana in Central America and Colombia and counter measures are under consideration. Options are limited, since products used need to have import tolerances in the US.

## 5. Mesotrione interim carry-over: Review

The topic had been discussed in detail at several meetings. D. Cornes, supported by J. Costello, J. Allen and M. Luczak provided an overview of the current state of knowledge.

Status and outlook for the 2004-'05 Season

- The weather conditions in 2004-5 look more favorable than in the previous season
- The Lumax submicron formulation will reduce future risk. However, 25% of sales in 2004 are still the old formulation
- Risk of carry-over is predicted to be lower than 2003-'04 and no pro-active measures are required. Label cut-off of June 1st remains valid
- Some late use (after June 1 label cut-off) in Wisconsin and Michigan due to wet conditions represent an increased risk; it is planned to run modeling at late dates for these states to define risks and advise reps if proactive action should be indicated.

Potential risk for consecutive applications

- The model shows a slight increase in the second year concentration; dry conditions result in slightly higher residues
- In the majority of soils - 2 consecutive applications, even in dry years, is unlikely to result in soybean damage
- The area at risk is low pH soils <pH 5.5 (<5% of acres)
- In these soils residues are higher after year 1 and slightly increase in year 2
- The increase after 2 years could result in increased soybean damage, but the area affected is very small, or could be patches of fields with low pH. The area at risk is predicted to be less than 0.08% of the total area planted to corn.

## Discussion and conclusions

Concern has now receded, although a small risk remains for some soils following a dry period during and just after the application. These situations will be monitored also in future and model predictions will provide early warning in case special measures should ever be indicated. The product has now worked very well with minimum adverse publicity for a number of years and has acquired a very positive and robust image. This is unlikely to be scratched by a few, isolated incidents should they ever occur.

The information we have gained will be useful in assessing the risk for similar products, but since soybean may react differently to compounds depending on variety, careful fieldwork will continue to be necessary.

The model will now be finalised and used to predict the risks for the 2005-'06 season. No further development should be required after August 2005.

The 2004-'05 trials comparing mesotrione acid and copper salt will be sampled in autumn and again at soybean planting time. The decision whether to continue formulation work will be taken in September '05.

- 5.1. Action: A final review of the status with a detailed analysis of the lessons learned and proposals for further action should be presented when the project is closed.

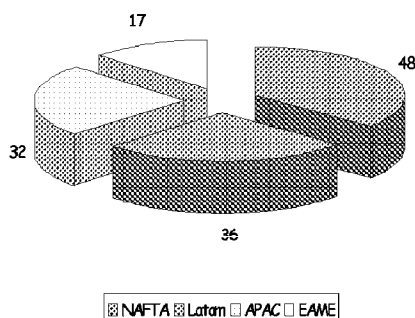
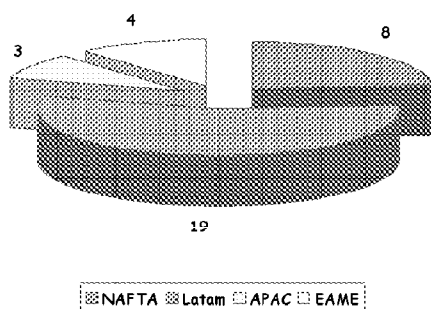
J. Barnes/DeCo 25.10.05

## 6. Ametryn registration in US: Status update

Ch. Harms, W. Maurer and J. Allen presented the topic, supported by M. Luczak

Sales forecast 2009 (\$m):

Gross Profit 2009 (%)



The US EPA is moving ahead with RED development in a 4-stage process:

- Stage 1: Technical "errors only" correction of preliminary risk assessments (completed Jan. 2005). Syngenta filed several "errors only" comments
- Stage 2: EPA acted upon Syngenta comments and made corrections (completed in Feb. 2005)
- Stage 3: 60-day public comment period on preliminary risk assessments (Feb. to Apr. '05) – all ametryn science documents made available to the public.
  - o Detailed evaluation and preparation of response continues; Syngenta plans to file extensive comments
- Stage 4: EPA review and revisions of risk assessments (expected May to Aug. 2005), leading to the final issuance of RED before Aug. 31 '05.

Options and likely impact:

Scenario	Regulatory and cost impact	Business impact
1. Maintain full US registration	<ul style="list-style-type: none"> <li>• short-/mid-term: Full costs</li> <li>• long-term: <ul style="list-style-type: none"> <li>- Maintains reg. in key OECD country</li> <li>- provides basis for reg. in other countries</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• mid-term: sustainable</li> <li>• long-term: sustainable</li> <li>• no impact on ATZ and PMY volumes</li> <li>• protects TSS business</li> </ul>
2. Maintain US import tolerances and AI registration	<ul style="list-style-type: none"> <li>• short-term: medium costs</li> <li>• mid-term: Full cost to maintain reg. in OECD countries (AU) &amp; LATAM</li> </ul>	<ul style="list-style-type: none"> <li>• mid-term: sustainable</li> <li>• long-term: support or phase-out?</li> </ul>
3. Drop US registration	<ul style="list-style-type: none"> <li>• short-term: minimal costs</li> <li>• mid-term: <ul style="list-style-type: none"> <li>- Need to maintain reg. in OECD country (AU)</li> <li>- PIC potential?</li> <li>- trigger addtl. work in BR</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• mid-term: Support or phase-out <ul style="list-style-type: none"> <li>- no export to US 2006+</li> <li>- reduced ATZ volume</li> <li>- impact on TSS (KRISMAT) and PMY (Codai Gold)</li> </ul> </li> </ul>

1. Maintain US registration: This option provides optimal freedom to operate. It would enable us to further develop the trifloxysulfuron business that depends on ametryn. Small domestic market.

This option does, however, demand the highest short-term investment as a set of studies need to be done to fill gaps and to meet the EPA Data Call In (DCI).

Expected development cost: \$4 to \$6 m

Total of sales maintained by 2014: \$35 m; NPV: \$29 m

2. Maintain US import tolerances for ametryn: Resource requirement are reduced since environmental fate, ecotox and operator exposure do not need to be covered. Most of the trifloxysulfuron business could be maintained.

The US sales would be lost and the ATZ & PMY volumes (COGS) at Agrilience could be impacted. Whilst the tech. AI registration remains valid, generic producers could still sell their product.

Expected development cost: \$3 to \$5 m

Total of sales maintained by 2014: \$27 m; NPV: \$25 m

Region NAFTA would like to maintain the registration in USA to maintain current sales of \$8 m and to avoid growers substituting atrazine at high rates. There is also strong US grower support for ametryn.

In Brazil ametryn is indispensable to develop the business in sugarcane – a market expected to grow in the medium-long term (production of gasohol)

## Discussion and conclusions

Full registration through EPA is not a foregone conclusion and a favorable outcome may be subject to a demanding DCI. Equally it is believed that there is a good chance (70%) that our argument concerning oncogenicity will be accepted and that a new study will not be needed. Any decision should still be revisited when comments are received in September, or when we know the scope of the DCI one year later.

The suggestion was made that this could be an opportunity for exploring whether placing the studies at an external laboratory would lead to a significant cost reduction. The idea received

support, but the point was made that any contract laboratory would have to meet minimum quality criteria and would also have to be acceptable to EPA.

- 6.1. Decision: The proposal to pursue Option 1 (maintaining the full US registration) is supported in principle. W. Maurer
- 6.2. Action: The team should review the project when the comments from EPA have been received and the data requirements are clearer. Significant investment must not be committed to before this has been done. J. Street/Q3'05
- 6.3. Action: Explore the merit of placing relevant studies externally. The objective would be to minimize the total cost of the programme. J. Street/Q4'05

## 7. Pyribenzoxim ( LG-40863): Project proposal for rice in Latam

The proposal was presented by J. Amrein, J. Allen, R. Kotzian, J. Schulze-Aurich, supported by M. Luczak

Syngenta does not currently have a competitive herbicide offer in direct seeded rice in South-east Asia and Latam. It is proposed to develop and sell a 3<sup>rd</sup> party product to capture this incremental business.

The opportunity: Post-em control of grasses and broad-leaved weeds in seeded rice

Submarket	Transplanted Rice	Seeded Rice	Trends
<b>Pre-plant &amp; Pre-emergence</b> <i>Grasses+</i>	\$85 m	\$ 100 m	<ul style="list-style-type: none"> <li>➤ Increasing in ISC</li> <li>➤ Declining in TP-rice (NEA)</li> </ul>
<b>Post-emergence</b> <i>Grasses + broad spectrum</i>	\$350 m	\$ 260 m	<ul style="list-style-type: none"> <li>➤ Increasing in seeded rice</li> </ul>
<b>Post-emergence</b> <i>Sedges + Dicots</i>	\$60 m	\$80 m	<ul style="list-style-type: none"> <li>➤ Stable generic SU-market</li> </ul>
<b>Totals</b>	<b>\$495 m</b>	<b>\$440 m</b>	

The market potential for pyribenzoxim is seen as \$100 m:

- \$75 m in APAC
- \$25 m in Latam

There is an up-side potential for a further \$20 - 30 m in Africa-Middle East, India and China. Market excluded from the agreement with LG represent a potential of \$130 m. This includes the US & EU (Reg-dossier not designed for these markets), Brazil and Ecuador (rights assigned to other partners) and Japan and South Korea (no technical fit).

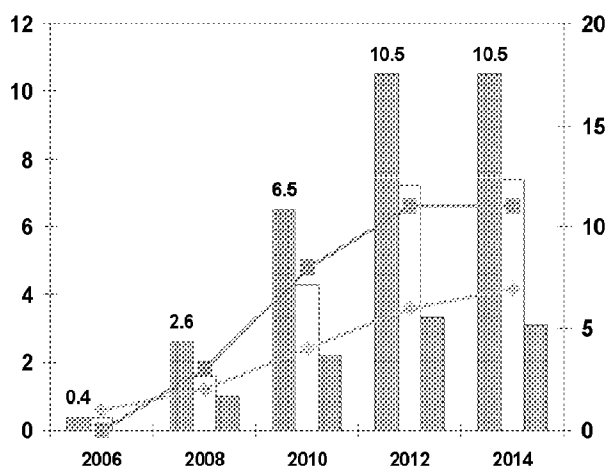
Expected competitive environment in the target markets at launch

AI	Brand Name	Sales M\$	M' Share %	Trend '04 - '09
Bis-pyribac	NOMINEE	25.8	17.8	↗
Butachlor/propanil	CHALLENGE/ var.	24.9	17.0	↔
- fop's	CLINCHER/var.	17.7	12.1	↔
- dim's	AURA/var.	7.0	4.8	↘
Pyribenzoxim	PYANCHOR	2.9	2.0	↗
Others		~20.0		↘
<b>TOTAL SUBMAR- KET</b>		<b>~\$100 m</b>		↗

Financial Objectives:

	GLOBAL (2006)	APAC/LATAM (2006)
1st Launch	2006	2006
Plateau Sales	7.5 m\$	3.0 m\$
Target %MS (treated area)	7 %	12 %
GP-Target	~40%	~45%

Sales build-up and market share:



The active ingredient:

Owner: LGLS (Korea)  
Trademark: PYANCHOR  
Pyrimidinyl-benzoate (ALS-inhibitor)  
Analogue to bis-pyribac (Trademark: NOMINEE)

GLOBAL Total	APAC	LATAM	APAC % MS	LATAM % MS
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The products:

Southeast Asia	Latam
direct seeded rice	direct seeded rice
<b>SOLITO EC 320</b> Formulated mixture with pretilachlor	<b>PYANCHOR EC 050</b> Solo Product from LGLS
VN, TH, PH, MY, SL, Africa	Columbia, Venezuela, Central America, Dom. Republic
<ul style="list-style-type: none"> <li>➤ <i>Formulation developed by SYN</i></li> <li>➤ <i>Formulation Safety Studies by SYN</i></li> <li>➤ <i>LoA for AI from LGLS</i></li> <li>➤ <i>Regulatory Process by SYN</i></li> </ul>	<ul style="list-style-type: none"> <li>➤ <i>Formulation developed by LGLS</i></li> <li>➤ <i>Registration Dossier from LGLS</i></li> <li>➤ <i>Few P&amp;C studies done by SYN</i></li> <li>➤ <i>Regulatory Process by SYN</i></li> </ul>

Technical Aspects:

Strengths:

- Timing-flexible post-emergence grass control in direct seeded rice
- Use rates between 30 and 50 g AI/ha
- Foliar active
- Controls most common grasses, BLW and Sedges in rice
- Selective in rice, cereals & turf

Limitations:

- No residual activity
- Low formulation loading
- Inconsistent performance on *Leptochloa* and *Ischaemum* grasses
- Good water-management needed
- Good soil leveling required

Registration Dossier:

- **Health Assessment:** Deficiencies in some AI studies
- Solo formulation: Eye irritation of concentrated product
- Toxicology: Low toxicity
- Operator Exposure: No undue risk to the operator under normal conditions of use; use of eye/face protection during mixing/loading (solo product)
- **E-Fate:** Deficiencies in some studies; no environmental risk expected
- **Ecotoxicology:** Deficiencies in some studies; high margin of safety
- **Dietary Safety:** Deficiencies in residue methods, validation and metabolism; zero residue situation - no risk to the consumer
- **Phys/Chem:** Specification to be defined; quality control to be set-up

Registration Plan:

LATAM Submissions 2005: Colombia, Venezuela, Dom. Republic  
Submissions 2006: Chile, Honduras, Guatemala, Belize, El Salvador

SEA Pyribenzoxim already/soon registered by LG  
Syngenta submissions 2005: Thailand, Malaysia, Vietnam, Philippines,  
Sri Lanka

### SWOT Analysis

Strengths	Weaknesses
<ul style="list-style-type: none"> <li>- Excellent grass activity incl. <i>Leptochloa</i></li> <li>- SOLITO combined contact- and residual activity</li> <li>- SOLITO superior broadleaf weed spectrum</li> <li>- Low pyribenzoxim AI rates</li> <li>- Favourable safety profile</li> </ul>	<ul style="list-style-type: none"> <li>- Late market entry by Syngenta</li> <li>- Similarity of PYANCHOR to NOMINEE</li> <li>- Incomplete market access (e.g. BR, NAFTA)</li> </ul>
Opportunities	Threats
<ul style="list-style-type: none"> <li>- Strong upside potential in APAC provided successful launch and technical superiority is confirmed</li> <li>- Technical fit for rice in Indian Subcontinent</li> <li>- Other rice markets (NAFTA) or crops (e.g. turf or vegetables) should be considered</li> </ul>	<ul style="list-style-type: none"> <li>- General price pressure by generics</li> <li>- Generic bis-pyribac (NOMINEE)</li> <li>- ALS weed resistance (mainly LATAM)</li> <li>- Relationship discontinuity with LGLS</li> </ul>

### Discussion and conclusions

The prospect of generating incremental sales in a segment where Syngenta has virtually not been present in the past appealed to most DeCo members. A small minority felt that our best plan would be to focus development resources on projects based on proprietary active ingredients, particularly since there were some doubts about the attractiveness of the target segment – one that had historically been dominated by cheap commodities.

The GL formulation appears rather old-fashioned and contains adjuvants we do no longer use. Also the fact that the formulation causes adverse eye effects even though the AI itself does not, is not attractive. It is accepted, however that because of the low solubility of the AI and the risk of delays, options for improvement may be limited and that stewardship plans may have to be made instead to manage the issue. Overall, the AI appears benign and there are no undue concerns related to either registration or the safety profile.

The project is well advanced and investment needs (< \$ 2m) are considered to be modest.

- 7.1. Decision: DeCo supports these two pyribenzoxim projects as proposed by the team. J. Amrein
- 7.2. Action: Regulatory and Stewardship should address the eye issue and either achieve a change in classification or plan appropriate stewardship measures. Current time lines should be adhered to. J. Street, R. Brown



**8. Decisions and Actions**

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2.1.	Decision: The proposed strategy is supported on the assumption that all new formulations meet existing hurdle criteria. J. Barnes.....	8
2.2.	Action: Further attention should be paid to the likely effect of generic imidacloprid on the development of resistance to neonicotinoids with a view to adjust our strategy as appropriate. K. Gehmann .....	8
2.3.	Action: Efforts should be undertaken to fully understand the implications of drip application for surface and ground water. H. Swaine .....	8
2.4.	Recommendation: Marketing is encouraged to consider the influence of the bisamids and the new Bayer sucking pest compound on sales forecasts. M. Stepan.....	8
2.5.	Action: Given the novelty of some of the new formulation concepts, careful consideration should be given to any opportunities to protect the intellectual property as it relates to our own, but also other manufacturers compounds. K. Gehmann .....	8
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